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REVISED 10/15/86

Microfiche No.		
0780519980		
New Doc I.D.	Old Doc I.D.	
86-870002190		
Date Produced	Date Received	TSCA section
1/29/65	9/04/87	8D
Submitting Organization		
DOW CHEMICAL		
Contractor		
INTL RESEARCH & DEVELOPMENT		
Document Title		
ACUTE INHALATION TOXICITY (LC50) IN THE MALE ALBINO RAT - PAPI, MDI (PURE, DISTILLED), MDI (PRE CUT, 3% OF TOTAL) AND BUNCO (N-BUTYL ISOCYANATE)		
Chemical Category		
N-BUTYL ISOCYANATE (111-35-4)		

International Research and Development Corporation

D 002125

SPONSOR: The Upjohn Company, Carwin Division
COMPOUNDS: PAPI Irrelevant, Filing Data
MDI, Pure, Distilled
MDI, Precut, 3% of Total
BUNCO (n-Butylisocyanate) m n 97.15
SUBJECT: Acute Inhalation Toxicity (LC50) in
the Male Albino Rat.

EPA-OTS



000049651P

86-870M 2190

CONTAINS NO CBI

SEP - 4 1987

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Date: January 29, 1965

203-004

7. SYNOPSIS

The test compounds were examined for acute inhalation toxicity (LC_{50}) using the male albino rat. All compounds were tested in the vapor form. Six rats for every concentration of each respective test agent were used.

An LC_{50} for PAPI could not be determined, since the physical constants of PAPI and the experimental protocol did not permit such a calculation.

While lethal levels were established for MDI, Pure, Distilled, an exact LC_{50} could not be calculated from the data. The approximate LC_{50} lies between 172 and 187 mcg./L.

The acute LC_{50} for MDI, Precut, 3% of Total, and for BUNCO were 4.4 and 15.2 mcg./L., respectively.

All results are expressed in terms of mcg./L. rather than ppm. due to the fact that the molecular weight of MDI, Precut, 3% of Total was not made available. The common expression of mcg./L. permits a comparison of the agents in terms of acute toxicity (LC_{50}) in the rat.

Pharmacodynamic and/or toxic effects, mortalities and necropsy data are documented in the body of this report.

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II. COMPOUNDS

The test compounds were received from the Upjohn Company, Carwin Division, North Haven, Connecticut, on August 24 and December 24, 1964.

Each of the four test compounds was sealed in a glass bottle and was identified as follows:

<u>Compound</u>	<u>Code No.</u>	<u>Description</u>
PAPI	2B-14-65	Dark brown viscous liquid
MDI, Pure, Distilled	---	Pale orange moist crystals
MDI, Precut, 3% of Total	---	Yellow-orange, moist semisolid
BUNCO (n-Butylisocyanate)	---	Straw-colored liquid

III. METHODS

A. General Procedure:

Male, albino rats of the Spartan Sprague-Dawley strain and weighing from 200 to 300 grams were used. The rats were individually housed in wire mesh cages elevated above the droppings and maintained in air-conditioned and humidity-controlled quarters throughout the pre-exposure and post-exposure periods. Food and water were available ad libitum except during the exposure period.

Body weights on all animals used were obtained prior to exposure to each respective agent and at 7 and 14 days after exposure.

All of the rats were observed for evidence of pharmacodynamic and/or toxic signs during the exposure period; for an additional period of several hours immediately after exposure; and daily for 13 days thereafter.

Animals which failed to survive the post-exposure observation period were necropsied and examined. All rats which survived to the termination of the 14-day observation period were sacrificed by means of an intraperitoneal injection of sodium pentobarbital and also necropsied and examined.

B. Compound Administration:

All of the compounds in these tests were analyzed in vapor form. This was accomplished by heating each respective compound in a flask on a water or oil bath at the desired temperature to produce vapors.

The vapors thus formed were carried into the exposure chamber containing the rats by use of an air source produced by a compressor. Prior to entrance into the evaporating flask containing the test agent, the air was passed through a glass wool filter and two drying tubes containing calcium chloride to clean and dry it.

The concentration of the vapors of each test agent carried by the inflowing air could be varied either by changing the volume of the inflow of air, or by altering the temperature of the bath producing the vapors, or as in the case of PAPI and BUNCO, by altering the speed of infusion of the test materials into the evaporating chamber with an infusion pump. Upon occasion, a second air source was introduced into the line carrying the vapors of a given agent into the exposure chamber to aid in further controlling the concentration of a given test material.

The rats were divided into groups of six animals each. One group was used at each respective concentration of each test agent analyzed.

For exposure purposes, a nine-liter air-tight chamber was used. All animals were exposed for one continuous hour to the vapors of each respective test agent.

1. PAPI:

This agent was injected into the distillation flask with a Harvard Infusion Pump (Model No. 600-910). The distillation flask was heated to a temperature of approximately $150 \pm 2^{\circ}$ Centigrade with an oil bath. The vapors thus formed were carried into the exposure chamber with a controlled inflow of air, as previously described, at 10 liters per minute.

Two groups of six rats each were thus exposed to analyzed concentrations of PAPI of 14.7 or 17.0 micrograms per liter (mcg./L.). Higher concentrations of PAPI could not be obtained by increasing the inflow of the compound with the infusion pump, and the degree of heat used could not be increased without exceeding the decomposition temperature of the agent. Furthermore, reduction of airflow produced

condensation (fallout) within the exposure chamber. Thus, only two concentrations of PAPI were analyzed.

The table below describes the experimental variables used in this test.

PAPI

Experimental Variables:

<u>Infusion Speed</u> <u>ml./min.</u>	<u>Oil Bath</u> <u>Temp. °C.</u>	<u>Airflow</u> <u>(L/M)</u>	<u>Analyzed</u> <u>Exposure Chamber</u> <u>Concen. (mcg./L.)</u>
0.194	150	10	14.7
0.494	150	15	17.0

2. MDI, Pure, Distilled:

MDI, Pure, Distilled was evaluated at analyzed concentrations of 0.6, 80.8, 162.0, 171.5, 186.6, 562.5 and 1530 mcg./L., using 6 rats at each respective concentration.

The vapor for the lowest concentration analyzed (0.6 mcg./L.) was produced by passing air through the test agent which was contained in a flask on an oil bath. The oil bath was maintained at a temperature of $100 \pm 2^\circ$ C. The airflow into the evaporating chamber was passed directly into the exposure chamber at a speed of one liter per minute.

All succeeding concentrations were produced in a similar manner, except that the test agent was heated to a temperature of approximately $200 \pm 2^\circ$ C. Airflow through the evaporating chamber was varied between 1 and 2 liters per minute. Further dilution of the air containing the vapors was accomplished with a second air source which was interposed into the system just prior to its entry

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into the exposure chamber. Airflow from this second source was varied from 0 to 10 liters per minute. By varying the airflow from the second source, the concentration of the vapors entering the exposure chamber could be controlled. The following table describes the experimental variables and the concentrations of MDI thus produced.

MDI, Pure, Distilled

Experimental Variables:

Oil Bath Temp. °C.	Airflow (Liters/Minute)			Analyzed Exposure Chamber Concen. (mcg./L.)
	Primary Source	Secondary Source	Total	
100	1.0	0.0	1.0	0.6
200	1.0	10.0	11.0	80.8
200	1.5	7.0	8.5	162.0
200	1.0	6.0	7.0	171.5
200	1.5	6.0	7.5	186.6
200	2.0	2.0	4.0	562.5
200	2.0	0.0	2.0	1530.0

3. MDI, Precut, 3 Per Cent of Total:

Using essentially the same technique as described above for MDI, Pure, Distilled, groups of 6 rats were exposed to analyzed concentrations of 2.4, 3.3, 6.7 or 11.8 mcg./L. of MDI, Precut.

The table below describes the experimental variables used in these tests.

MDI, Precut, 3% of Total

Experimental Variables:

Oil Bath Temp. °C.	Airflow (Liters/Minute)			Analyzed Exposure Chamber Concen. (mcg./L.)
	Primary Source	Secondary Source	Total	
200	1.0	10.0	11.0	2.4
200	1.0	8.0	9.0	3.3
200	1.0	7.0	8.0	6.7
200	1.5	6.0	7.5	11.8

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4. BUNCO (n-Butylisocyanate):

As in the case with PAPI, the test agent, BUNCO, was infused into a 150 mm. U-tube by use of a Harvard Infusion Pump, Model No. 600-910.

Except at the first (lowest) concentration of BUNCO used, the 150 mm. U-tube was immersed in a water bath which was maintained at a constant temperature of $80 \pm 2^{\circ} \text{C}$.

Clean, dried air was passed through the U-tube containing BUNCO and the speed of inflow was varied as necessary to modify the concentration of vapor passing into the exposure chamber. The concentration of the vapor was further modified by altering the rate of infusion of the test agent into the U-tube with the infusion pump.

Using the method described, 9 groups of 6 rats each were exposed to the vapors of BUNCO at analyzed concentrations varying from 5.5 to 34.6 mcg./L. of air. The table below describes the experimental variables used to control exposure chamber concentrations of BUNCO.

BUNCO (n-Butylisocyanate)

Experimental Variables:

<u>Infusion Speed</u> <u>(ml./min.)</u>	<u>Water Bath</u> <u>Temp. ° C.</u>	<u>Airflow</u> <u>(Liters/min.)</u>	<u>Analyzed</u> <u>Exposure Chamber</u> <u>Concen. (mcg./L.)</u>
0.00136	-	10	5.5
0.0034	80	10	7.9
0.0051	80	10	10.9
0.0068	80	10	12.0
0.0103	80	12	18.9
0.0103	80	10	21.7
0.0136	80	10	27.9
0.0136	80	10	28.2
0.0340	80	10	34.6

C. Analytical Methods (Table 1)

Prior to the exposure of the animals to varying concentrations of each test agent, calibration curves were prepared for each substance by the following method: Serial dilution of a known concentration of each respective test agent in the reagent (0.5 per cent p-dimethylaminobenzaldehyde in 50 per cent glacial acetic acid) were prepared. After maximum color development had occurred, each dilution was read in a Coleman spectrophotometer at a wave length of 425 millimicrons, using a reagent blank to balance the instrument.

The optical densities thus obtained were plotted against the concentrations in mcg./ml. for each test agent. The resultant curves obtained were used to determine the concentration in mcg./L. of subsequently obtained samples of atmospheric concentrations from the exposure chamber of each agent during a given exposure.

The individually prepared concentration curves of each test agent obtained as described appear in Table 1.

Samples were collected from the exposure chamber by absorption into a midget impinger containing 25 ml. of the reagent (0.5 per cent dimethylaminobenzaldehyde in 50 per cent glacial acetic acid). Sampling from the chamber was maintained constant for all of the test agents at 0.5 liters of airflow per minute. The length of the sampling time continued until development of color in the reagent had occurred.

IV. RESULTS

A. Pharmacodynamic and/or Toxic Signs:

1. PAP1:

a. 14.7 and 17.0 mcg./L.:

All rats at both concentrations of PAP1 appeared essentially normal throughout the one-hour exposure period and the 14-day post-exposure observation period. Slight salivation and erythema were observed during the exposure period in both groups of rats. All rats at both concentrations used survived the 14-day observation period.

2. MDI, Pure, Distilled:

a. 0.6 mcg./L.:

Signs seen during the exposure included a general slight erythema and restlessness. Five-of-six exhibited slight salivation and 2-of-6 showed slight nasal porphyrin discharge. All rats in this group appeared normal the following day and remained so until necropsy.

b. 80.8 mcg./L.:

During the exposure the rats exhibited salivation, excessive lacrimation and clear nasal drip, dyspnea, escape behavior, and slight nasal porphyrin discharge. No signs were seen from the day following the exposure until necropsy. All rats survived the 14-day observation period.

c. 162 mcg./L.:

Signs seen during this exposure were similar to those seen at the 80.8 mcg./liter level, but appeared among the rats much earlier, and were more marked at the termination of the exposure. Again, all 6 rats appeared essentially normal

from the day following the exposure until necropsy and all survived the observation period.

d. 171.5 mcg./L.:

Signs recorded during this exposure included those noted above at lower concentrations, plus a slight increase in activity during the initial few minutes. One-of-six rats showed marked nasal porphyrin at the termination of the exposure. All rats appeared essentially normal from the day following the exposure until necropsy and all survived to termination of the test period.

e. 186.6 mcg./L.:

In addition to the salivation, excessive lacrimation, clear nasal drip, and dyspnea, previously mentioned, an increase in grooming activity, and eye-squint were seen during this exposure. At the termination of this exposure, all rats exhibited salivation and dyspnea, and 3-of-6 showed muscle flaccidity. Three-of-six rats died overnight after the exposure. The day following the exposure, 1-of-3 showed dyspnea and nasal and ocular porphyrin, and 2-of-3 showed hypoactivity. The 4th mortality occurred 26 hours after the exposure. From the 2nd post-exposure day on, the 2 survivors appeared essentially normal.

f. 552.5 mcg./L.:

Within 10 minutes after initiating this exposure, the exposure chamber was completely filled with "fog". Marked ptyalism, dyspnea, eye-squint, excessive lacrimation, and increased grooming were recorded. In addition, after 55 minutes, the eyes appeared dark and the exposed skin (ears and paws) appeared cyanotic. Inspection of the rats immediately after the exposure revealed

dyspnea, salivation and cyanosis, all of which lasted throughout the balance of the day. Six-of-six mortalities occurred overnight.

g. 1530.0 mcg./L.:

During this exposure, the test chamber again became filled with "fog" during the first few minutes. Gross observations were similar to those recorded for the 562.5 level. Eye-squint advanced to eye-closure and the dark appearance of the eyes and the cyanotic condition of the exposed skin was seen during exposure and at termination of the exposure period. Three-of-six died during the exposure, and the remaining 3 rats within one hour thereafter.

3. MDI, Precut, 3 Per Cent of Total:

a. 2.4 mcg./L.:

Pharmacodynamic and/or toxic signs observed during the one-hour exposure period at this concentration included lacrimation, salivation, increased grooming activity, escape behavior and dyspnea. After exposure, hypoactivity and labored respiration continued. On the day following exposure, dyspnea was still in evidence. The animals exhibited rough coats and nasal porphyrin discharge. One mortality occurred on the 1st post-exposure day and one on the 2nd day. The 4 remaining rats survived the remainder of the 14-day post-exposure period.

b. 3.3 mcg./L.:

This group of rats displayed essentially the same signs as noted above at the 2.4 mcg./L. concentration. In addition to those signs noted, moist rales were prevalent in this group for 48 hours after exposure. One rat died within 6 hours after exposure. The remaining 5 rats survived the 14-day observation period.

c. 6.7 mcg./l.:

The signs observed in this group was essentially the same as those previously noted, but were somewhat more intense in degree. Four rats in this group died within 24 hours. The remaining 2 rats survived the 14-day observation period.

d. 11.8 mcg./l.:

All rats in this group displayed those signs noted above and all died within 4 hours after exposure to the test agent at this concentration.

4. BUNCO (n-Butylisocyanate):

Pharmacodynamic and/or toxic signs observed at the varying concentrations of BUNCO employed generally were dose-related in severity and included hypoactivity, increased grooming activity (during exposure only), salivation, lacrimation, dyspnea, escape behavior (during exposure only) and death.

Mortalities at the lower concentrations of BUNCO were delayed. While these were few in number and variable in occurrence, the calculations of an LC_{50} were influenced considerably by the deaths. In order to obtain a valid LC_{50} value, the method of Reed and Muench¹ was used. This method tends to equalize chance variations. After finding the percentage deaths, these were plotted on log probability paper and the method of Litchfield and Wilcoxon² was used to calculate the final LC_{50} and the confidence limits.

The mortality data for BUNCO appears in Table 3.

¹ L. J. Reed and H. Muench: *Am. J. Hyg.* 27: 493, 1938.

² J. T. Litchfield, Jr. and F. Wilcoxon: *J. Pharmacol. Exptl. Therap.* 96: 99, 1949.

B. Body Weights (Table 2):

1. PAPI:

Rats exposed to an analyzed atmospheric concentration of PAPI of 14.7 mcg./L. showed essentially normal body weight gains. Those rats at the 17.0 mcg./L. level showed a very slight inhibition of body weight gain during the first week only.

2. MDI, Pure, Distilled:

Rats exposed to an analyzed concentration of 0.6 mcg./L. of MDI, Pure, Distilled, showed normal body weight gain during the 2-week period of observation. However, the average body weight gain for the surviving rats of the other 6 groups exposed to the vapors of this agent appeared to be inhibited for the first week.

3. MDI, Precut, 3 Per Cent of Total:

The average body weight for surviving rats in the groups exposed to vapors of the agent showed a less-than-normal gain for the first week following exposure. During the 2nd week, however, group average body weight gains appeared normal.

4. BUNCO (n-Butylisocyanate):

The group of rats exposed to BUNCO vapors at an analyzed concentration of 5.5 mcg./L. showed essentially normal average body weight gain. Marked body weight losses were seen for the surviving rats from the other 8 groups. In general, the surviving rats continued to lose body weight during the 2nd post-exposure week.

C. Necropsy Examination:

1. Mortalities:

Necropsies made on those rats that died during the 2-week period of observation revealed the following:

a. PAPI:

No Mortalities.

b. MDI, Pure, Distilled:

(1) 186.6 mcg./L.: Four-of-four exhibited hydrothorax and lungs with edema and congestion; 1-of-4, lungs with severe hemorrhages.

(2) 562.5 mcg./L.: Six-of-six showed hydrothorax and lungs with generalized congestion and edema.

(3) 1530.0 mcg./L.: Six-of-six showed lungs with severe generalized hemorrhage and edema throughout.

c. MDI, Precut, 3 Per Cent of Total:

(1) 2.4 mcg./L.: One-of-two, lungs with severe hemorrhage and edema; 1-of-2, hydrothorax and lungs with severe congestion and edema.

(2) 3.3 mcg./L.: Single mortality showed lungs with severe congestion and edema.

(3) 6.7 mcg./L.: Four-of-four, lungs with hemorrhage and edema; 1-of-4, hydrothorax.

(4) 11.8 mcg./L.: Six-of-six, lungs with severe congestion and edema; 2-of-6, hydrothorax.

d. BUNCO (n-Butylisocyanate):

(1) 7.9 mcg./L.: The one mortality showed inflated lungs with hemorrhages throughout.

(2) 10.9 mcg./L.: One-of-two, lungs which remained inflated and with a 10 mm. area of consolidation.

(3) 18.9 mcg./L.: Five-of-six rats that died within one day after exposure showed lungs with edema and severe

hemorrhages. The 6th mortality occurring the 13th day after exposure was autolyzed.

(4) 21.7 mcg./L.: Four-of-four, lungs with severe hemorrhages; 1-of-4, lungs inflated and fluid in trachea; 1-of-4, autolysis.

(5) 27.9 mcg./L.: Six-of-six, hydrothorax and lungs with severe hemorrhages; 4-of-6, tympany of the stomach.

(6) 28.2 mcg./L.: Six-of-six, lungs with severe hemorrhages; 5-of-6, hydrothorax and lungs with edema.

(7) 34.6 mcg./L.: Six-of-six, lungs with severe hemorrhages and edema; 4-of-6, hydrothorax.

2. Survivors:

Necropsies made on those rats which survived the 2-week period of observation revealed the following:

a. PAPI:

(1) 14.7 mcg./L.: Four-of-six, no gross lesions; 1-of-6, lung with 2 mm. dark area; 1-of-6, lungs with 6 mm. areas of congestion.

(2) 17.0 mcg./L.: Four-of-six, no gross lesions; 2-of-6, lungs with 6-10 mm. areas of congestion.

b. MDI, Pure, Distilled:

(1) 0.6 mcg./L.: Four-of-six, no gross lesions; 2-of-6, lungs with 10 mm. areas of congestion.

(2) 80.8 mcg./L.: Five-of-six, no gross lesions; 1-of-6, lung with 6-15 mm. areas of hyperemia.

(3) 162 mcg./L.: One-of-six, no gross lesions; 2-of-6, lungs with 2 mm. red foci; 1-of-6, lungs with two 6 mm. areas of congestion.

(4) 171.5 mcg./L.: No gross lesions seen.

(5) 186.6 mcg./L.: One-of-two, no gross lesions; and 1-of-2, a lung with a 2 mm. red foci.

c. MDI, Precut, 3 Per Cent of Total:

(1) 2.4 mcg./L.: Three-of-four showed no gross lesions; and 1-of-4 showed lungs with 10-15 mm. areas of hyperemia and a 2 mm. dark area.

(2) 3.3 mcg./L.: Three-of-five showed no gross lesions; 1-of-5, lung with 5 mm. area of consolidation; 1-of-5, lung with two 1 mm. dark red areas.

(3) 6.7 mcg./L.: The 2 rats that survived until necropsy showed no gross lesions.

d. BUNCO (n-Butylisocyanate):

(1) 5.5 mcg./L.: Four-of-six, no gross lesions; 1-of-6, lung with 8 mm. areas of congestion; 1-of-6, lung with two 8 mm. hemorrhages.

(2) 7.9 mcg./L.: The mortality showed inflated lungs with hemorrhages throughout. Of the 5 survivors, 5-of-5 showed lungs which remained inflated after sacrifice, and an involuted thymus; 4-of-5 showed trachea and bronchi that contained a small amount of mucus; 1-of-5, stomach with edema and hemorrhages, and lung with two 2 mm. dark areas; 1-of-5, lungs with 6 mm. area of consolidation; and 1-of-5, absence of body fat.

(3) 10.9 mcg./L.: Four-of-four, lungs which remained inflated after sacrifice; 3-of-4 showed absence of abdominal fat, an involuted thymus, and fluid throughout the small intestine; 2-of-4 showed paraphimosis.

(4) 12.0 mcg./L.: Terminal necropsies revealed: 6-of-6, lungs inflated after sacrifice; 2-of-6, lungs with consolidation; 1-of-6, lungs with 10-15 mm. areas of congestion; 1-of-6, lungs with 2-3 mm. dark areas; 1-of-6, lungs with 10 mm. area of hyperemia; and 1-of-6, trachea with a small amount of mucus..

(5) 21.7 mcg./L.: Two-of-two, inflated lungs, an absence of abdominal fat, and involution of the thymus. One-of-two, lungs with 3 mm. dark foci; 1-of-2, lungs with consolidation and fluid throughout the gastrointestinal tract.

D. Acute Inhalation Toxicity (LC₅₀):

1. PAPI:

It was not possible to achieve an LC₅₀ for PAPI.

2. MDI, Pure, Distilled:

Data obtained from the exposures of 7 groups of 6 rats each to 7 different analyzed atmospheric concentrations of MDI, Pure, Distilled vapors does not permit the calculation of an LC₅₀. However, inspection of the levels employed and the mortalities obtained reveals that the LC₅₀ is approximately 170 mcg./L.

3. MDI, Precut, 3 Per Cent of Total (Table 3 and Figure 1):

The calculated LC₅₀ for this compound was found to be 4.4 mcg./L. with confidence limits of 2.8 - 6.8 mcg./L.

4. BUNCO (n-Butylisocyanate) (Table 3 and Figure 1):

The calculated LC₅₀ for BUNCO was found to be 15.2 (12.1 - 19.0) mcg./L.

E. Analytical Results:

The analysis of the actual chamber concentrations of the agents used in these studies at the various concentrations employed were obtained by interpolation from the values appearing in Table 1. In actual practice, graphs were constructed for each individual agent by plotting the data appearing in Table 1. Actual concentrations in the exposure chamber were calculated by obtaining optical densities of 425 millimicrons as previously described under methods, entering the table at the respective density obtained and reading the concentration indicated.

Acute Inhalation Toxicity Studies in the Rat.

TABLE 1. Calibration Curves.

Compound	Optical Densities																
	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50	0.55	0.60	0.65	0.70	0.75	0.80	0.85
	Concentration, mcg./ml.																
PAPI	0.30	0.53	0.75	1.00	1.27	1.50	1.77	2.00	2.26	2.54	2.90	3.30	3.77	4.37	5.25	6.20	-
MDI, Pure	0.10	0.19	0.30	0.40	0.53	0.62	0.77	0.90	1.04	1.22	1.40	1.58	1.77	2.00	2.35	3.00	4.25
MDI, Precut	0.14	0.28	0.42	0.57	0.71	0.85	1.00	1.20	1.43	1.68	1.93	2.31	2.82	3.50	-	-	-
BUNCO	11.0	18.5	26.0	33.8	41.5	49.0	56.7	65.0	75.0	87.5	98.5	-	-	-	-	-	-

Acute Inhalation Toxicity Studies in the Rat.

TABLE 2. Average Body Weights, Grams.

Test Compound Concentration (mcg./L.)	Control	7 Days	14 Days
<u>PAPI:</u>			
14.7	217	271	301
17.0	261	274	304
<u>MDI, Pure, Distilled:</u>			
0.6	223	279	303
30.8	273	277	323
162.0	263	282	319
171.5	272	274	323
186.6	268	259 ^a	305 ^a
562.5	292	-	-
1530.0	289	-	-
<u>MDI, Precut, 3 Per Cent of Total:</u>			
2.4	272	273 ^c	328 ^c
3.3	264	251 ^d	300 ^d
6.7	264	268 ^a	320 ^a
11.8	268	-	-
<u>BUNCO (n-Butylisocyanate):</u>			
5.5	267	299	323
7.9	262	213 ^d	196 ^d
10.9	272	229	195 ^c
12.0	262	206	216
18.9	270	219 ^b	-
21.7	276	213 ^b	183 ^z
27.9	269	-	-
28.2	293	-	-
34.6	264	-	-

a - 2 rats only

b - 3 rats only

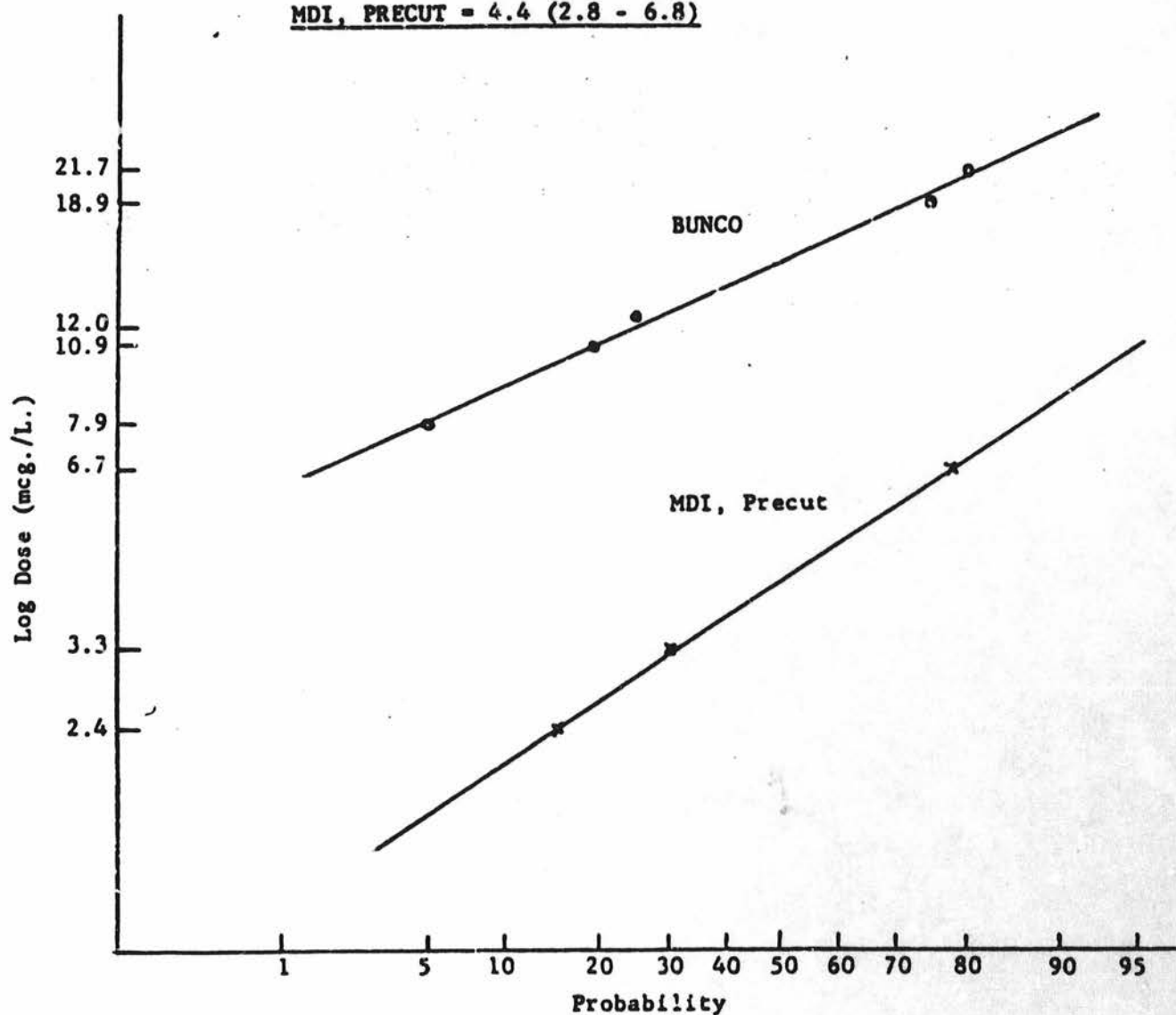
c - 4 rats only

d - 5 rats only

Acute Inhalation Toxicity Studies in the Rat.

TABLE 3. Mortality Data in the Male Albino Rat.

Analyzed Atmospheric Concentration mcg./L..	Time of Death - Days Post-Exposure No. Died/No. Exposed														Total	LC50 and Confidence Limits (mcg./L.)	
	0	1	2	3	4	5	6	7	8	9	10	11	12	13			14
PAPI:																	
14.7																0/6	None sible
17.0																0/6	
MDI, Pure:																	
0.6																0/6	Approximately 178
80.8																0/6	
162.0																0/6	
171.5																0/6	
186.6	3/6	1/3														4/6	
562.5	6/6															6/6	
1530.0	6/6															6/6	
MDI, Precut:																	
2.4		1/6	1/5													2/6	4.4 (2.8 - 6.8)
3.3	1/6															1/6	
6.7		4/6														4/6	
11.8	6/6															6/6	
BUNCO:																	
5.5																0/6	15.2 (12.1 - 19.0)
7.9		1/6														1/6	
10.9									1/6					1/5		2/6	
12.0																0/6	
18.9			5/6													6/6	
21.7			2/6											1/1		4/6	
27.9	2/6	4/4							1/4	1/3						6/6	
28.2	1/6	5/5														6/6	
34.6	6/6															6/6	

Figure 1. Mortality Data of BUNCO and MDI, PRECUT.LC₅₀: BUNCO = 15.2 (12.1 - 19.0)MDI, PRECUT = 4.4 (2.8 - 6.8)

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CERTIFICATE OF AUTHENTICITY

THIS IS TO CERTIFY that the microimages appearing on this microfiche are accurate and complete reproductions of the records of U.S. Environmental Protection Agency documents as delivered in the regular course of business for microfilming.

Data produced 2 20 89 Barbara Smith
(Month) (Day) (Year) Camera Operator

Place Syracuse New York
(City) (State)

